IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS	: Simons *et al.*
SERIAL NO.	: 09/145,916
FILED	: September 2, 1998
FOR	: "STIMULATION OF ANGIOGENESIS VIA ENHANCED ENDOTHELIAL EXPRESSION OF SYNDECAN-4 CORE PROTEINS"
EXAMINER	: David Guzo
GROUP ART UNIT	: 1636
ATTORNEY'S DOCKET NO.	: BIS-039

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commission for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on: July 19, 2004

Attorney for applicants: David Prashker

Signature: [signature]

Date: July 19, 2004

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MARKED UP VERSION OF AMENDED SPECIFICATION SUBMITTED
PURSUANT TO 37 C.F.R.1.121(b)(1)(iii)

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

Applicants, in fulfillment of and in accordance with the requirements of 37 C.R.F. 1.121(b)(1)(iii), hereby submit a marked up

version of amendments to the Specification which appear at the following location:

Page 14, lines 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23 respectively; and

Page 15, line 2.

Respectfully submitted,

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Date: July 19, 2004

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Fig. 1 is a representation of a prepared DNA sequence fragment;

Fig. 2 is a recitation of the DNA sequence coding for the extracellular domain of syndecan-1 [SEQ ID NO:1];

Fig. 3 is a recitation of the DNA sequence coding for extracellular domain of syndecan-2 [SEQ ID NOS:2 & 3];

Fig. 4 is a recitation of the DNA sequence coding for the extracellular domain of syndecan-3 [SEQ ID NO:4];

Fig. 5 is a recitation of the DNA sequence coding for the extracellular domain of syndecan-4 [SEQ ID NO:5];

Fig. 6 is a recitation of the DNA sequence coding for the extracellular domain of glypican- 1 [SEQ ID NOS:6 & 7];

Fig. 7 is a recitation of the DNA sequence coding for the transmembrane domain of syndecan-1 [SEQ ID NO:8];

Fig. 8 is a recitation of the DNA sequence coding for the transmembrane domain of syndecan-2 [SEQ ID NOS:9 & 10];

Fig. 9 is a recitation of the DNA sequence coding for the transmembrane domain of syndecan-3 [SEQ ID NO:11];

Fig. 10 is a recitation of the DNA sequence coding for the transmembrane domain of syndecan-4 [SEQ ID NO:12];

Fig. 11 is a recitation of the DNA sequence coding for the transmembrane domain of GP1 [SEQ ID NOS:13 & 14];

Fig. 12 is a recitation of the DNA sequence coding for the transmembrane domain of perlecan [SEQ ID NO:15];

Fig. 13 is a recitation of the DNA sequence coding for the cytoplasmic domain of syndecan-4 [SEQ ID NO:16];

Fig. 14 is a graph illustrating the in-vitro growth assays of ECV-derived cell clones;

Figs. 15A-15C are photographs showing the results of Matrigel growths assays;

Fig. 16 is a graph illustrating the effect of syndecan construct expression on endothelial cell migration in Boyden chamber assays;

Figs. 17A-17F are photographs showing BudR uptake in opiop homozygous *(-/-)* and heterozygous *(+1-)* mice;

Fig. 18 is a photograph showing Northern blot analysis of gene expression in PR-39 transgenic mice; and

Fig. 19 is a graph illustrating in-vitro microvascular reactivity in PR-39 transgenic mice.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides both the tangible means and the methods for causing an overexpression of extracellular, heparan sulfate carrying, proteoglycans on-demand at and through the surface of endothelial cells; and via such on-demand overexpression of proteoglycans to stimulate angiogenesis in-situ. The tangible means include a prepared DNA segment comprising sequences coding for an extracellular domain, a transmembrane domain, and the cytoplasmic domain of the